REMARKS/ARGUMENTS

Reconsideration is respectfully requested. Claims 1-3, 6-14 and 16-21 are pending. Claims 4, 5, and 15 have been canceled. Claims 1-3, 8, 10, 13, and 19 have been amended. Claims 11, 12, 16-18, and 21 have been withdrawn. Amendments to the claims do not add new matter and do not affect the inventorship.

Applicants have not dedicated or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections made by the Patent Office. Applicants reserve the right to pursue prosecution of any presently excluded claim embodiments in future continuation and/or divisional applications.

Amendments to the Specification

The second full paragraph on page 6 to the second paragraph on page 7 has been amended to correct the informalities. The arrow is re-written in text form as suggested by the Examiner. The section tiled "Detailed Description of the Invention" which runs from page 14 to page 16 has been amended for clarity. Table 1 on pages 35 and 36 is made into new Figures 20a and 20b in the Drawings. The figure legend is moved to the end of the section titled "Detailed Description of the Invention." Pages 35 and 36 are deleted accordingly. No new matter is added due to the amendments.

Amendments to the Drawings

Figure 15 has been amended. The first two graphs have been deleted, and the third and fourth graphs have been numbered "a" and "b" accordingly. Figure 16 has been amended to add panel numbers "a" and "b". New Figures 20a and 20b have been added, which correspond to Table 1 on pages 35 and 36 as originally filed. No new matter is added due to the amendments.

Claim Amendments

Claims 1 and 3 have been amended to recited "An isolated mutant human serum albumin having at least 90% sequence identify to native human serum albumin." Support is found, for example, in original claim 4.

Claims 2, 8, 10, and 19 have been amended for technical clarity.

Claim 3 has been amended to call for the specific positions in each of the sequences

shown in Table 1. Support is found, for example, in page 4, first paragraph, which discloses the residues at each X_n positions of human serum albumin which can be used to locate the positions of those X_n in Table 1 ("Human serum albumin comprises the sequence identified above, wherein X_1 is H, X_2 is N, X_3 is H, X_4 is D, X_5 is Y, X_6 is L, X_7 is G, X_8 is E, X_9 is H, X_{10} is H and X_{11} is H.") Therefore, no new matter is added.

Claim 13 has been amended to correct antecedent basis.

Election/Restrictions

The Examiner has reiterated the Restriction Requirements in the instant Office Action. However, Applicants have already elected Group I (claims 1-10, 13, 19, and 20) in the previous response as acknowledged by the Examiner in the instant Office Action. Applicants respectfully request clarification.

Objection to the Specification

The Examiner objects to the specification because of various formalities.

a) The specification on pages 6 and 7 is objected to because of the use of arrows. The specification has been amended to rewrite in the text form as suggested by the Examiner.

b) The specification on pages 35 and 36 is objected to because of the insertion of Table 1. Table 1 has been made into Figure 20a and Figure 20a of the Drawings as suggested by the Examiner.

c) The Examiner objects to the description of the drawings. Description of Figure 1 has been amended to refer to the "boxed area" which is clear from the Drawings. Description of Figure 3c and 8 has been amended to delete the references related to color in the Drawings. Description of Figure 14 has been amended to remove the references of a-e. Panel numbers have been added in Figures 15 and 16 in the amended Drawings.

With the amendments to Specification and the Drawings, Applicants believe all informalities have been corrected and respectfully request the objections be withdrawn.

Objection to the Claims

a) Claim 1 is objected to for improper punctuating the sequence identifier. Claim 1 has been amended to delete the extra period. Claim 1 also been amended to remove the sequence as suggested by the Examiner.

b) Claim 8 is objected to for the use of arrows. Claim 8 has been amended as

suggested by the Examiner.

c) Claim 10 is objected to because the spacing between "Asn" and "99His" should be deleted. Claim 10 has been amended to correct the informalities.

d) Claim 2 has been objected to because on the alleged basis of the lack of clarity with regard to the relationship between the mutants and the change of the physical characteristic. Claim 2 has been amended to correct the informalities.

Applicants believe the claim amendments overcome all the objections and respectfully request the objections be withdrawn.

Claim Rejections -35 USC §112

Claims 1-10, 13, 19 and 20 stand rejected under 35 USC §112, second paragraph, as being indefinite.

a) Claims 1, 3, and 19 are rejected on the alleged basis "that it is not clear whether the physiological characteristics with respect to native human serum albumin are altered or not."

Without acquiesce to the propriety of the rejections, Claims 1, 13, and 19 have amended to recite "altered physiological characteristics". Applicants believe the amendments obviate the rejections and respectfully request the rejections be withdrawn.

b) Claim 3 is rejected on the alleged basis that it refers to a Table 1.

Claim 3 has been amended to recite the sequence listed on Table 1 by sequence identification numbers, thus obviate the rejections. Applicants respectfully request the rejection be withdrawn.

c) Claims 1 and 3 (and claims dependent thereof) are rejected on the alleged basis that "the phrase 'substantially comprising' in reference to an isolated mutant serum albumin does not reflect the percent of identity of the mutant to the native peptide."

Claims 1 and 3 have been amended to delete the phrase "substantially." Applicants submit the amendments obviate the rejections and respectfully request the rejections be withdrawn.

d) Claim 4 is rejected on the alleged basis as being indefinite. Claim 4 has been amended, rendering the rejection moot.

However, the Examiner also states that "because nowhere in the claims or in the disclosure the native sequence of human serum albumin is defined. Thus, is impossible to clearly define 90% identical sequence." Applicants respectfully disagree.

The limitation "having at least 90% sequence identify to native human serum albumin" has been included in amended claim 1. The specification discloses on page 3 an isolated mutant human serum albumin sequence and discloses on page 4, first full paragraph that: "Human serum albumin comprises the sequence identified above, wherein X_1 is H, X_2 is N, X_3 is H, X_4 is D, X_5 is Y, X_6 is L, X_7 is G, X_8 is E, X_9 is H, X_{10} is H and X_{11} is H." As such, the specification clearly discloses the sequence of human serum albumin. Table 1 in original pages 35 and 36 also discloses the sequence of human serum albumin (SEQ ID NO:2) and its Accession number in the GenBank is p02769.

e) Claim 5 stands rejected as being indefinite. Claim 5 has been canceled, rendering the rejection moot.

f) Claim 10 stands rejected on the alleged basis that "because a mutant serum albumin is claimed with a mutation of Asn99His, Asn99Asp, or His67Ala, however there is no SEQ ID NO assigned to such a mutant."

Claim 10 has been amended to refer to SEQ ID NO:1. Applicants submit the amendments obviate the rejections and respectfully request the rejections be withdrawn.

g) Claim 13 stands rejected on the alleged basis of lacking clear antecedent basis to claims 1 or 3.

Claim 13 has been amended. Applicants submit the amendments obviate the rejections and respectfully request the rejections be withdrawn.

Claim Objections -35 USC §112

Claims 1-10, 13, 19, and 20 stand rejected under 35 USC §112, first paragraph, for failing to comply with the written description and enablement requirements. Applicants respectfully traverse.

Written Description

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. M.P.E.P. § 2163.

The written description requirement for a claimed genus may be satisfied through (1) sufficient description of a representative number of species by actual reduction to practice, (2) reduction to drawings, or (3) by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled

with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus . M.P.E.P. § 2163.

Applicants submit Claims 1 and 3 (and claims dependent therefrom) as amended meet the written description requirement.

First, the specification provides ample description of representative species by actual reduction to practice. For example, page 6 and 7 discloses the numerous mutants where a residue at one of the position X_n is changed, and the actual reduction to practice of numerous mutants, such as His67Ala, Asn99Asp and Asn99His. See page 23.

The specification also discloses identifying characteristics, including both the structural and functional properties. For example, the specification discloses that the metal binding affinity is altered in the mutants, see page 6, and the mutants cause the change of cell adhesion and/or growth, see page 7.

The specification further discloses the correlation between the function and the structure. For example, the specification discloses positions that can be mutated to generate mutants with altered metal binding affinity. See page 6.

Accordingly, the present application provides sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. Applicants respectfully request the rejections be withdrawn.

Enablement

Any analysis of whether a particular claim is supported by the disclosure in an application requires a determination of whether that disclosure, when filed, contained sufficient information regarding the subject matter of the claims as to enable one skilled in the pertinent art to make and use the claimed invention without undue experimentation. M.P.E.P. § 2164.01.

Applicants submit Claims 1 and 3 (and claims dependent therefrom) as amended meet the enablement requirement.

First, Claims 1 and 3 (and claims dependent therefrom), as amended, require the structure of the claimed mutants to have "at least 90% sequence identity" to the native serum albumin from which such mutants are derived. Claims 1 and 3 further require the claimed mutants have at least one mutation at one of the 11 positions recited.

Secondly, the specification discloses both the methods of making the claimed mutants

and methods to assay the functional characteristics of the claimed mutants. The specification discloses the method of site-directed mutagenesis that is used to generate the claimed mutants, see page 8, third paragraph to page 9, second full paragraph. The specification further discloses methods of determining the functional characteristics of the mutant, such as the metal binding affinity by NMR, see page 8, first paragraph and page 19-21, and cell viability caused by the mutant, see page 22-23.

Finally, the specification discloses numerous examples of the mutants as described in the Examples.

As such, the specification provides sufficient disclosure to enable a skilled artisan to make the claimed mutant by site-directed mutagenesis and test for the functional characteristics of the claimed mutants.

Accordingly, the present application provides sufficient information regarding the subject matter of the claims as to enable one skilled in the pertinent art to make and use the claimed invention without undue experimentation. Applicants respectfully request the rejections be withdrawn.

Claim Objections -35 USC §102

Claims 1, 3, 6-8, 13, and 19 stand rejected under 35 USC §102 as being anticipated by Sargent et al., (Accession No. P02770) ("*Sargent*") as evidenced by Anderson et al. (Bioseparation 2, pages 15-22, 1991) ("*Andersson*"). Applicants respectfully traverse.

For an anticipation rejection under 35 U.S.C. § 102 to be proper, a single reference must disclose each and every element of a claim. *In re Paulsen*, 31 USPQ2d 1671, 1673 (Fed. Cir. 1994); M.P.E.P. § 2131 (citing *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989).

Claim 1, as amended, calls for "An isolated mutant human serum albumin having at least 90% sequence identity to native human serum albumin and comprising the amino acid sequence of SEQ ID NO:1"

In contrast, the sequence disclosed in *Sargent* is wild-type rat serum albumin, which is only 78.3% identical to the human serum albumin. Therefore Claim 1 does not read on *Sargent* and is not anticipated by *Sargent*.

Claim 3, as amended, calls for "An isolated mutant mammalian serum albumin having at least 90% sequence identity to the native mammalian serum albumin from which the mutant is derived and comprising one of the sequences of SEQ ID NOs:2-10." Claim 3, as

amended, further requires that at least one of the residues at the recited positions be mutated.

In contrast, the sequence disclosed in *Sargent* is wild-type rat serum albumin, and does not have the residues mutated at the specific positions required by Claim 3. Therefore Claim 1 does not read on *Sargent* and is not anticipated by *Sargent*.

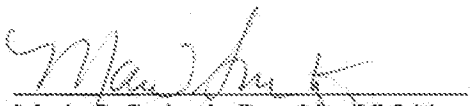
The Examiner also cites *Andersson*, which relates to immobilized metal ion affinity chromatography of serum albumins. Specifically, *Andersson* describes interaction of albumins with various divalent imino-diacetate-chelated metal ions, including zinc, immobilised on a chromatography column. It is noted that although a "high-affinity" site for zinc is mentioned in the paper, the authors do not present experimental data that would specify or identify the residues involved in zinc binding, other than speculating that two histidine residues might be involved. The authors suggest mutating residues His145, His336, His9, His18, His508 and His533 in bovine albumin. However, none of these are identical to histidines that the present inventors have identified as being the "true" zinc ligands, such as His67 and His247 according to the sequence of SEQ ID NO:1.

For the foregoing reasons, Claims 1 and 3 (and claims dependent therefrom) are not anticipated by *Sargent* as evidenced by *Andersson*. Applicants respectfully request the rejection be withdrawn.

CONCLUSION

In light of the above amendments and remarks, the Applicant respectfully requests that the Examiner reconsider this application with a view towards allowance. The Examiner is invited to call the undersigned attorney at (650) 843-4000, if a telephone call could help resolve any remaining items.

Respectfully submitted,



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under 37 C.F.R. §1.34

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